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Division of Dockets Management
U.S. Food & Drug Administration
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5630 Fishers Lane Room 1061
Rockville, MD 20857

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Docket 2005N-0038
Novartis comments on Reporting Averse Events to Institutional Review Boards

April 20, 2005

Dear Sir/Madam:

Novartis Pharmaceuticals Corporation (Novartis) is an affiliate of Novartis AG (NYSE: NVS), a world leader in pharmaceuticals and consumer health. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 81,400 people and operate in over 140 countries around the world.

Novartis researches, develops, manufacturers and markets leading innovative prescription drugs used to treat a number of diseases and conditions, including central nervous system disorders, organ transplantation, cardiovascular diseases, dermatological conditions, respiratory disorders, cancer and arthritis.

The March 21st, 2005 public hearing revealed a general consensus that distribution of adverse event (AE) information to Institutional Review Boards (IRBs) could be improved. More specifically, presenters at the meeting expressed universal concern that the current volume of AE reports detracts from straightforward and rapid interpretation of safety data by IRBs. Most favored a process whereby individual AEs are summarized in periodic reports prepared by study sponsors. The attendees felt that only those AEs with a potential to significantly impact a compound's safety potential should be distributed as individual alerts.

Novartis believes all aspects of trial conduct should function under transparent processes for data collection, monitoring and reporting to optimize patient care and foster positive outcomes. To improve IRB notification, we agree that summary information can better facilitate patient safety, and support in principle revising current regulatory guidance. Novartis advocates incorporating the recommendations of CIOMS Working Group VI (*Management of Safety Information from Clinical Trials*) into future FDA guidance on IRB reporting. Adoption of these recommendations would include the following:

- Discontinuing the routine practice of sending large numbers of individual AE reports to investigators, who in turn report these to their respective IRBs.
- Replacing the process with periodic (e.g. quarterly) and *ad hoc* contextual summaries of safety information and evolving benefit-risk profiles.
- *Ad hoc* communications could be triggered by a single AE report that may impact trial conduct or warrant an immediate change to informed consent or aggregate information, e.g., pre-clinical or clinical study results, which bring significant new safety information and have implication for the conduct of the trial.

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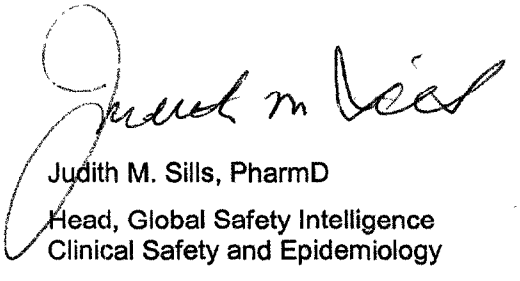
- The format for periodic summaries should be similar to that described in CIOMS VI section 7.c(3).
- The criteria for issuing an *ad hoc* report should be similar to those described in CIOMS VI section 7.c(3).

In addition, Novartis wishes to make the following comments.

- New regulatory guidance should not require a level of data interpretation by sponsors that will lead IRBs to pre-determined conclusions. Rather, sponsors should provide adequate data to allow these groups to make their own informed assessments. The focus of the process should be increasing the ability of IRBs to process and analyze information effectively and efficiently. If, however, it is the intent of the guidance for sponsors to scientifically interpret the data first, that expectation should be clearly stated.
- The information provided by sponsors to IRBs should be the same in context as that sent to regulators. Sponsors should not filter information based on pre-conceived judgments of the recipients' areas of study involvement and needs.
- Any new guidance on this topic should offer general expectations for communication format and structure. Ideally, IRB notifications might reflect an existing or proposed universal format, such as that recommended in CIOMS VI. Companies should be allowed to provide comments and suggestions before such guidance is finalized.
- New roles and responsibilities defined in the guidance should also take into account the impact on IRB members and investigators with respect to time commitment, training needs, and resource availability.
- The new EU Clinical Trials Directive has already taken a different approach from FDA to reporting from clinical trials. Novartis strongly recommends that FDA and the EU develop a harmonized approach to reporting AEs from clinical trials, and consider using the ICH process to accomplish this.
- It would be useful for sponsors to know FDA's thinking on handling investigator-initiated protocols in the context of this issue.

If you have any questions regarding these comments, please contact Mr. Thomas Umrath at (862) 778-2293.

Sincerely,



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